DEPARTMENT OF THE ARMY

CHEMICAL BIOLOGICAL MEDICAL SYSTEMS JOINT PROJECT MANAGEMENT OFFICE

BROAD AGENCY ANNOUNCEMENT

MEDICAL CHEMICAL BIOLOGICAL RADIOLOGICAL AND NUCLEAR COUNTERMEASURE RESEARCH AND DEVELOPMENT

AREAS OF INTEREST

BAA 07-01

AUGUST 2007

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FREDERICK, MARYLAND

CHEMICAL BIOLOGICAL MEDICAL SYSTEMS JOINT PROJECT MANAGEMENT OFFICE

BAA 07-01

PREFACE

Medical Chemical, Biological, Radiological and Nuclear (CBRN) countermeasures are an integral part of the U.S. Department of Defense (DoD) Chemical Biological Defense Program (CBDP) System of Systems approach that serves as the foundation and strength of the CBDP. The Joint Program Executive Office for Chemical and Biological Defense (JPEO-CBD) is organized into eight Joint Project Management Offices, each responsible for specific commodity areas. The Chemical Biological Medical Systems Joint Project Management Office (CBMS JPMO) consists of the Joint Vaccine Acquisition Program (JVAP), Medical Identification and Treatment Systems (MITS), and Transformational Medical Technologies Initiative (TMTI) Joint Product Management Offices (JPMOs). The medical CBRN countermeasures developed by the CBMS JPMO directly support the current, near-term, and far-term challenges by providing the capability to prevent, diagnose and treat the effects of chemical, radiological and biological warfare agents. The JVAP JPMO provides biological protection by ensuring Warfighters' immune systems are primed to protect them from selected threats. The MITS JPMO is responsible for the advanced development of U.S. Food and Drug Administration (FDA)-approved/licensed/cleared products for prophylaxis, treatment and diagnosis of CBRN agent exposure. The TMTI JPMO is developing and evaluating novel processes to accelerate the development and approval of medical CBRN countermeasures by leveraging lifecycle bioinformatics, enabling technologies, and other emerging technologies. General information on JPEO-CBD and subordinate JPMOs can be obtained from the JPEO-CBD website at http://www.jpeocbd.osd.mil/.

This Broad Agency Announcement (BAA) is intended to solicit pre-proposals for: 1) those parts of development not related to the development of a specific system or hardware procurement in accordance with (i) the Federal Acquisition Regulation (FAR) 35.016(a) and (ii) DoD Grant Regulations (DoDGARs) subject to section 2374 of Title 10 United State Code and 2) the development of prototypes in accordance with Section 845 of Public Law (P.L.) 103-160. The purpose of this BAA is to identify the best available science, and as such, there are no set-asides associated with any awards resulting from this BAA. Specific areas of interest are described in the "Areas of Interest" attachment. As to any resultant procurement contracts, this BAA is issued under the provisions of the Competition in Contracting Act of 1984 (P.L. 98-369), as implemented in the FAR at accordance. This Announcement provides a general description of the JPEO-CBD and CBMS JPMO's project areas, including specific areas of interest, general information, evaluation and selection criteria, and proposal preparation instructions. All Attachments that are required with the submission of a full proposal are described in the Mandatory Proposal Forms section of this announcement. **Proposals are sought from all eligible sources, including educational institutions, nonprofit organizations, and private industry. Generally, this announcement is continuously open; preliminary proposals**

(preproposals) may be submitted and will be evaluated at any time throughout the year. The availability of funds may limit the ability of the U.S. Government to make awards in specific areas, nevertheless preproposals are sought under this BAA announcement for all areas of interest described in the "Areas of Interest".

This announcement of the U.S. Government's current interests will be posted on the Grants.gov web portal (http://www.grants.gov/), the Federal Business Opportunity website (http://www.fedbizopps.gov), and the JPEO-CBD website. From time to time, this BAA may be amended with announcements or calls for proposals. Additionally, the application process may be amended as other electronic application processes are implemented. All amendments to this BAA will be announced on the JPEO-CBD website, the Grants.gov web portal, and the Federal Business Opportunity website.

White papers pertaining to grant proposals should not be submitted prior to August 15, 2007.

To facilitate communication on both scientific and administrative matters relating to this BAA, a single email address may be used for all communication with the JPEO-CBD and CBMS JPMO. Please send all technical and administrative questions and inquiries to cbmsbaa@amedd.army.mil.

Potential applicants are encouraged to discuss their proposal ideas with the CBMS technical staff. In addition to the address above, potential applicants may discuss their ideas with the Technical Contacts listed at the end of each area of interest.

Administrative questions concerning the preparation of preproposals or proposals should be addressed to U.S. Army Space and Missile Defense Command (USASMDC)/CBMS JPMO Grants Officer. They should be emailed to cbmsbaa@amedd.army.mil, faxed to 301-619-5069, ATTN: BAA 07-01, or mailed to the following address:

Chemical Biological Medical Systems
ATTN: BAA 07-01
64 Thomas Johnson Dr.
Frederick, MD 21702

Issues with submitting applications through the Grants.gov web portal should be directed to the Grants.gov help desk at 1-800-518-4726 or email support@grants.gov. The Contact Center hours of operation are Monday-Friday, 7 AM to 9 PM Eastern Standard Time.

The Catalog of Federal Domestic Assistance (CFDA) can be accessed online at http://www.cfda.gov. The online CFDA provides access to a database of all Federal programs available to the grant community, including state, local and tribal Governments, academia and research institutions, commercial firms and not-for-profits. Included on the web site are contact information for the office that administers each program, instructions on how to apply for assistance, and several proposal writing guides. The CFDA number for this announcement is 12.360.

CHEMICAL BIOLOGICAL MEDICAL SYSTEMS JOINT PROJECT MANAGEMENT OFFICE

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ACRONYMS

BAA	Broad Agency Announcement
BLA	Biologics License Application
BWA	Biological Warfare Agents
CBDP	Chemical Biological Defense Program
CBMS JPMO	Chemical Biological Medical Systems Joint Project Management Office
CBRN	Chemical, Biological, Radiological, and Nuclear
CFDA	Catalog of Federal Domestic Assistance
CFR	Code of Federal Regulations
cGMP	current Good Manufacturing Processes
CWA	Chemical Warfare Agents
CWVD	Chemical Warfare Vapor Detectors
DoD	Department of Defense
FAR	Federal Acquisition Regulation
FDA	U.S. Food and Drug Administration
GLP	Good Laboratory Practices
IND	Investigational New Drug
JPEO-CBD	Joint Program Executive Office for Chemical and Biological Defense
JVAP JPMO	Joint Vaccine Acquisition Program Joint Product Management Office
MITS JPMO	Medical Identification and Treatment Systems Joint Product Management Office
MRC	Medical Radiation Countermeasure

NDA	New Drug Application
NIOSH	National Institute of Occupational Safety and Health
NTA	Non-Traditional Agents
OT	Other Transaction
OTA	Other Transaction Authority
P.L.	Public Law
RDT&E	Research, Development, Test, and Evaluation
TIC	Toxic Industrial Chemical
TMTI JPMO	Transformational Medical Technologies Initiative Joint Product Management Office
TRL	Technology Readiness Level
USASMDC	U.S. Army Space and Missile Defense Command
USC	U.S. Code

BACKGROUND

GENERAL COMMENTS

The Joint Program Executive Office for Chemical and Biological Defense (JPEO-CBD) is the Joint Services principal advocate and single focal point for research, development, acquisition, fielding and life-cycle support of chemical and biological defense equipment, systems, and medical countermeasures.

Within the Joint Program Executive Office, eight Joint Project Managers (JPMs) lead, manage, and direct the acquisition and fielding of chemical, biological, radiological and nuclear (CBRN) detection and reconnaissance systems, individual and collective protection systems, decontamination systems, information management systems, medical devices, drugs, and vaccines, and installation and force protection systems.

Located throughout the United States, each JPM office leverages the talents and expertise from across the services under a single chain of command, providing the best chemical and biological defense program (CBDP) technology, equipment and medicine at the right cost, at the right place and at the right time.

The Joint Program Executive Officer (JPEO) provides intensive centralized management of assigned medical and non-medical programs to expedite material solutions for validated CBDP deficiencies. The JPEO monitors technology based activities to promote and facilitate transfer, acceleration, and insertion of emerging technologies to user applications across the military services.

The JPEO supports all military services to include homeland defense, allies, and U.S. citizens and troops abroad. The JPEO establishes and sustains responsive CBDP life cycle management; implements acquisition reform, focused on the use of best practices; maximizes knowledge, technology, and industrial base viability by partnering with government, academic, and commercial organizations to achieve optimal capabilities; enhances user satisfaction to retain and expand its user base; and maximizes employee potential.

This BAA sets forth areas of interest of the JPEO and JPMS

DEFINITIONS

Advanced research. Advanced technology development that creates new technology or demonstrates the viability of applying existing technology to new products and processes in a general way. Advanced research is most closely analogous to precompetitive technology development in the commercial sector (i.e., early phases of research and development on which commercial competitors are willing to collaborate, because the work is not so coupled to specific products and processes that the results of the work must be proprietary). It is typically funded in

Advanced Technology Development (Budget Activity 3 and Research Category 6.3A) programs within Research, Development, Test and Evaluation (RDT&E).

Applied research. Efforts that attempt to determine and exploit the potential of scientific discoveries or improvements in technology such as new materials, devices, methods and processes. It typically is funded in Applied Research (Budget Activity 2 and Research Category 6.2) programs within RDT&E. Applied research normally follows basic research but may not be fully distinguishable from the related basic research. The term does not include efforts whose principal aim is the design, development, or testing of specific products, systems or processes to be considered for sale or acquisition; these efforts are within the definition of "development."

Basic research. Efforts directed toward increasing knowledge and understanding in science and engineering, rather than the practical application of that knowledge and understanding. Basic research is typically funded within Basic Research (Budget Activity 1 and Research Category 6.1) programs within RDT&E.

Development. The systematic use of scientific and technical knowledge in the design, development, testing, or evaluation of potential new products, processes, or services to meet specific performance requirements or objectives. It includes the functions of design engineering, prototyping, and engineering testing. Advanced development consists of activities that plan, produce and deliver information outputs (documents, data, and records) from discovery all the way through Phase 4 post-marketing studies and surveillance. The general phases of the lifecycle are discovery, preclinical and clinical phases

Enabling Technologies. Technologies that are not countermeasure products or systems themselves but facilitate or accelerate the development of countermeasure products or systems. Examples of enabling technologies include combinatorial chemistry, high-throughput screening, microarrays, bioinformatics and computational biology, nanotechnologies, and imaging (including biosensors and biomarkers).

Health Surveillance. The ongoing, systematic collection, analysis, and interpretation of health-related data to detect and assess health risks in order to plan, implement, and evaluate prevention and intervention/response programs. Included are computational models, such as expert systems and predictive models.

Improved Logistics Tracking. Technologies which facilitate tracking and monitoring individual product items throughout shipping, storage, delivery to, and use by the end user (factory to foxhole). For example, technologies which facilitate or simplify cold chain management and/or shelf life extension.

Joint Project Manager (JPM). The designated individual with responsibility for and authority to accomplish program objectives for development, production, and sustainment to meet the user's operational needs. The JPM is accountable for credible cost, schedule, and performance reporting to the MDA.

Life Cycle Bioinformatics. The systematic collection and analysis of data from all phases of research, development, manufacturing, and test and evaluation to enable informed decision making. Included are data obtained from preclinical studies, ensuring compliance with 21 Code of Federal Regulations (CFR) part 11, phase 4/post-marketing studies and product surveillance.

Milestone Decision Authority (MDA) (JPEO-CBD). The designated individual with overall responsibility for the Chemical and Biological Defense Program. The MDA has the authority to approve entry of an acquisition program into the next phase of the acquisition process and shall be accountable for cost, schedule, and performance reporting to higher authority, including Congressional reporting.

THE JOINT PROGRAM EXECUTIVE OFFICE FOR CHEMICAL AND BIOLOGICAL DEFENSE PROGRAMMATIC MISSION AREAS

JPM Biological Defense: Develops, produces, fields and sustains world-class biological defense technology and equipment for the Joint Services. In partnership with the civilian sector, academia and industry, the JPM-BD will ensure that its biological defense products and services are developed at the best possible time, and can be sustained in operation at the lowest life cycle cost.

JPM NBC Contamination Avoidance: The Joint Project Manager for Nuclear, Biological, and Chemical Contamination Avoidance is responsible for the development, production, integration, testing, and fielding of NBC detection, obscuration, and reconnaissance systems. We ensure that our system developments, integration efforts and services focus on the Joint Warfighters' needs within cost, schedule, and performance parameters.

JPM Collective Protection: In Support of the National Military Strategy, research, develop, procure, field, dispose of, and provide sustainment guidance for Collective Protection equipment and systems that protect personnel and equipment within protected areas from chemical, biological, radiological, and toxic industrial materials.

JPM Decontamination: The Joint Project Manager Decontamination (JPM, Decon), Joint Program Executive Office for Chemical and Biological Defense (JPEO-CBD) is responsible for providing US Forces the capability to sustain operations in a contaminated environment with the least necessary burden and minimum degradation to mission accomplishment.

JPM Guardian: To provide integrated non-conventional and conventional weapon defense capabilities for installation protection and support to civilian authorities

JPM Individual Protection: The JPM IP develops, tests, procures and fields state of the art garments, masks, boots and gloves to protect the Warfighter from chemical, biological and radiological threats. The JPM-IP is the principal advocate and single point of contact for all

acquisition efforts within the Department of Defense for individual protection of chemical and biological threats.

JPM Information Systems: The mission of the Joint Project Manager for Information Systems is to provide the information architecture and applications for shaping the battle space against the chemical and biological threat. The Joint Project Manager for Information Systems provides the war fighter with integrated early warning capability, an accredited hazard prediction model, state-of-the-art consequence management, and course of action analysis tools.

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JPM Chemical and Biological Medical Systems: The Chemical Biological Medical Systems Joint Project Management Office (CBMS-JPMO) is responsible for the development, procurement, fielding, and sustaining of premier medical protection and treatment capabilities against chemical and biological warfare agents. Our products are all submitted through the U.S. Food and Drug Administration (FDA) licensing or approval processes. The mission of CBMS JPMO is to develop and field FDA-approved medical CBRN countermeasures for the Warfighter. We are seeking proposals in support of this overarching mission. We are interested in proposals that are based on data from experiments using specific CBRN agents, not surrogates, to demonstrate safety, efficacy or mode of action. We are interested in ways to develop medical CBRN countermeasures more rapidly and with increased efficiency through enabling technologies, life cycle bioinformatics, and improved logistics tracking. We are not interested in proof-of-concept, advanced, applied or basic research proposals. We are interested in efforts directed toward the development of enabling technologies that speed up the advanced development process leading to FDA approval. All developmental efforts nominated to be considered by this BAA should be evaluated against the Technology Readiness Levels (TRL) for Medical Product Development (Appendix A). Potential developmental efforts must be consistent with the minimum criteria at TRL level 3-4 for transition to advanced development.

BIOLOGICAL MEDICAL PROPHYLAXIS

Biological Medical Prophylaxis provides medical countermeasures against biological warfare agents. These countermeasures include specialized medical materiel (e.g., vaccines, antivirals, antitoxins, immunotherapeutics) as well as other biological products (e.g., immunoglobulins) designed to be effective as prophylaxis or, to treat rare but serious adverse events from other prophylaxis treatments. Biological Medical Prophylaxis countermeasures must be FDA-approved to provide the Joint Force with the ability to protect Warfighters from the debilitating and life threatening health threats of biological warfare agents (bacteria, viruses, and biotoxins) prior to the appearance of symptoms, thereby protecting Warfighters, conserving the strength of forces, and reducing the impact on the medical care system.

Biological Medical Prophylaxis countermeasures should protect against battlespace challenge of biological warfare agents (BWA) (e.g., aerosol exposure), be deliverable by minimally invasive means in as few doses as feasible, provide protection as quickly as possible, maintain protection as long as possible, be effective against a broad spectrum of agents, and be flexible enough to respond to a wide range of agents, including genetically altered agents. Biological Medical Prophylaxis countermeasures should limit the logistic burden on the force through limited special storage or handling requirements, reduced dosing, administration, and monitoring requirements. These capabilities must also provide for insertion of technology upgrades and commonality of components to address changing threats.

Biological Medical Prophylaxis technologies must be in advanced development, either preclinical or at the clinical evaluation stage of development. Ideally, products should be ready for Investigational New Drug (IND) application to the FDA, or already in or beyond Phase 1 clinical safety trials.

Overarching priorities of the Biological Medical Prophylaxis program include:

1. Develop prophylaxis or pretreatment systems to protect Warfighters from the effects of biological warfare agents prior to the appearance of symptoms. Primary prevention through vaccination is generally preferred as a long term goal, where possible and supported by the nature of the agent. Vaccine development is historically a difficult, expensive, and time-consuming effort. Vaccines are agent, and frequently subtype specific. For these reasons, there is particular interest in broad spectrum protection and multi-agent medical products.

    a. Vaccine development which focuses on protection from agents in aerosol exposure, molecular approaches for development of vaccines, measurement of relevant cellular and humoral protective immune responses, and expression or production of protective antigens using recombinant technology.

    b. Vaccine development for specific toxins and disease agents which could involve the generation, selection and characterization of attenuated strains or inactivated purified antigen preparations, to include polyvalent vaccines that are more broadly effective.

    c. Safer means of passive immunization, such as production of human monoclonal or modified antibodies that are despeciated.

2. Prevention, treatment or supportive care regimens for adverse reactions to prophylaxis or pretreatments. Some vaccines or other pretreatments occasionally result in adverse reactions that require treatment themselves, such as in the case of smallpox vaccine. In such circumstances, an immune globulin or other biological or drug product is required to be part of the vaccine or product "system" to prevent or treat rare but potentially serious adverse events. FDA approval is required for these associated products.

3. Enabling technologies that support, facilitate, or accelerate the development or licensure of Biological Medical Prophylaxis countermeasures.

a. Identification of correlates of protection for the agents described above and development of assays to assess such protection.

b. Development/characterization of relevant animal models to meet FDA licensing requirements for biodefense biologics.

c. Development of improved methods for delivery of vaccines, including adjuvants, nucleic acid vaccines, methods for oral or nasal immunization with inactivated, live and subunit antigens; sustained release formulations; and methods for delivery of antigens for specific induction of mucosal immunity and development of methods to enhance appropriate immune responses to include co-delivery of cytokines.

Infectious agents of interest to the Biological Medical Prophylaxis program include Ebola virus, Marburg virus, poxvirus models of variola virus and those agents causing Venezuelan equine encephalitis, western and eastern equine encephalitis, Tularemia, Q-fever, and Brucellosis. Toxins of interest include those from plants (ricin), bacteria (Staphylococcal enterotoxins, botulinum toxin serotypes C, D, E, F, G), and membrane damaging toxins.

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MEDICAL CHEMICAL DEFENSE

Prophylactic/pretreatment and therapeutic pharmaceuticals, for the purpose of this BAA, are *pharmacological* or *biological* products used to prevent or treat patients exposed to chemical warfare agents (CWA). The products will be licensed or approved by the FDA for their intended use, potentially to include juvenile, geriatric, or immunocompromised patients. Treatment of chemical casualties depends on effective use of multiple medical capabilities in an integrated manner. Warfighters may use self-administered pharmaceuticals or administer pharmaceuticals to another Warfighter. Health care providers must have appropriate pharmaceuticals, tools to diagnose and monitor response of casualties, and appropriate means to protect themselves from chemical hazards. We are particularly interested in developing medical chemical countermeasures that are active against a broad spectrum of chemical agents. Chemical agents of concern fall under the broad categories of nerve, blister, blood, and pulmonary agents.

Overarching goals of the Medical Chemical Defense project include:

1. Develop systems that support maintenance or restoration of pre-CWA exposure health and that allow Warfighters to complete their mission. This includes medical CWA countermeasures that prevent, reverse, or significantly mitigate the effects and negative operational impact of CWA. Medical CWA countermeasures may block the effects of CWA, stop or reverse the direct effects of those agents, or prevent or treat the pathology and symptoms of chemical agents. Specific areas of interest include:

    a. Drug treatment strategies to control seizures produced by nerve agents and protect against the neurological sequelae.

b. CWA pretreatments, prophylactics, or scavengers that can protect the Warfighter from nerve agent exposure and afford protection without physiological side effects.

c. Safe and effective cutaneous prophylactics and therapeutics to treat vesicant (blister) CWA injuries.

2. Develop medical CWA countermeasures that provide broad-spectrum prevention or treatment for classes of chemical agents and a range of exposure routes. Threats from chemical agents are likely to become more complex in the future as a result of increased agent variety and sophistication. Therefore, the products should be flexible enough to respond to a wide range of agents, including traditional and emerging agents. Medical CWA countermeasure systems might also include developing therapies and protocols for treatment that mitigate agent persistence or special effects of new threat agents, such as those that can potentially penetrate protective clothing.

3. Evaluate and leverage enabling technologies to enhance/prolong the shelf life of nerve agent countermeasures currently in the military arsenal. Areas of interest include developing new container-closure systems, wet-dry autoinjectors or formulation development.

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MEDICAL RADIOLOGICAL COUNTERMEASURES (MRC)

The goal of the MRC project is to select, develop, and manufacture FDA-approved drugs and biologics to increase survival and decrease incapacity by treating the incipient or manifest radiation injury following exposure to radiation from nuclear or radiological weapons so that Warfighters can maintain operational effectiveness. MRC must be safe, efficacious, free of performance-degrading side effects, compatible with current military CBRN countermeasures, and usable while in combat or garrison, during medical evacuation, and in hospital. Desired, but not mandatory, product attributes include ease of administration (e.g., autoinjector) and administrable to subjects wearing military protective gear, efficacy with a single dose or short course of treatment, and retained efficacy even if delivered more than 24 hours after radiation exposure. MRC should not require refrigeration or have other significant logistical burdens and should have a relatively long shelf life. These requirements are derived from the "CBRN Agents Therapeutic Pharmaceuticals Initial Capabilities Document," dated July 18, 2005 (JROCM 155-05). *Excluded from consideration under this BAA are candidate MRC which require use prior to exposure (i.e., prophylaxis) and next generation antibiotics and probiotics, blocking, decorporation, and purgative agents, antiemetics and other comfort or supportive measures.*

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MEDICAL DIAGNOSTIC SYSTEMS

The DoD has a need for technologies for the detection, identification, and clinical diagnosis of infection by pathogens and toxins with the potential to negatively impact force health and effectiveness. Sensitivity, specificity, ease of use, and deployability (size, weight, power requirements, reduced consumables) are critical features of such systems. An integrated system using multiple technology approaches that will reduce the potential for misdiagnosis of a BWA or other disease agent in clinical samples will provide the solution for future diagnostic capabilities. Specific areas of interest include:

1. Increase the capability of current diagnostic systems via the addition of functional modules.

2. Technologies or concepts which will decrease system size, weight, procurement and life cycle cost, logistics footprint, and training requirements.

3. Cross-over technologies such as diagnostics applicable to both clinical diagnosis of disease caused by both BWA and militarily-relevant infectious diseases and environmental monitoring (including the detection of food-borne pathogens).

4. Population health monitoring including a) real-time, b) predictive models, and c) expert systems.

5. Novel nucleic acid-based assays for BWA to include clinical, food, and environmental samples.

6. Novel non-nucleic acid-based assays for BWA, food pathogens, and toxins, including but not limited to immunoassays or novel detection reagents (e.g., antibodies or non-antibody recognition reagents).

7. Technologies or methods for the detection of pathogens and toxins of DoD interest, including BWA, that reduce or eliminate the need for analyte-specific reagents.

8. Systems or methods for analytical sample preparation compatible with nucleic acid-based (DNA and RNA) and non-nucleic acid-based detection methods, with emphasis on simplified methods that enrich and concentrate target analytes. Manual and automated systems are of interest, with a particular focus on automated methods that can be integrated with analytical platforms.

9. Methods for stabilizing analytical reagents at room temperature (e.g., 22-28° C and elevated temperatures up to 50° C).

10. Development and validation of host response biomarkers of infection or disease that permit diagnosis of infection while still in the presymptomatic or very early symptomatic phase when intervention is most likely to be effective.

11. Development of assays for validated host response biomarkers of infection or disease that are compatible with, and can be transitioned to, potential next generation diagnostic technologies.

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JPEO/ CBMS JPMO CATEGORIES OF INTEREST FOR THIS BAA

CATEGORY 1. MEDICAL CBRN COUNTERMEASURE PROTOTYPES

To obtain and develop the best Medical CBRN Countermeasure technologies, regardless of their source, the CBMS JPMO is contemplating the use of Prototype OTs for the purpose of developing medical CBRN Countermeasure prototypes. Nontraditional defense contractors, including large pharmaceutical companies, are eligible to submit a proposal for medical CBRN countermeasure prototype development under this BAA.

A nontraditional defense contractor is a business unit that has not, for a period of at least one year prior to the date of the OT agreement, entered into or performed on (1) any procurement contract that is subject to full coverage under the cost accounting standards prescribed pursuant to section 26 of the Office of Federal Procurement Policy Act (41 USC 422) and the regulations implementing such section; or (2) any other procurement contract in excess of $500,000 to carry out prototype projects or to perform basic, applied, or advanced research projects for a federal agency.

For a candidate medical CBRN Countermeasure to be eligible for consideration for development through FDA approval as a prototype under this BAA, it must be the subject of an active IND application with the FDA that is not on clinical hold. The IND may be for an indication other than the indication to be obtained as part of the proposed effort. The advanced development of a MRC requires the capability to build the necessary processes to select, develop, validate and manufacture a drug or biologic in accordance with FDA current Good Manufacturing Practices (cGMP) regulations and guidelines. **Therefore, medical CBRN countermeasure prototype proposals (and white papers/preproposals) submitted in response to this BAA must provide substantiated *in vivo* safety and efficacy data arising from the study of the proposed CBRN countermeasure candidate, evidence of compliance with cGMP, and evidence of good management skills and practices.**

1. Advanced development of MRC prototypes through FDA approval. This effort may include clinical safety studies, pivotal efficacy studies, small and large scale manufacturing, and the preparation and submission of a New Drug Application (NDA) or Biologic License Application (BLA) to the FDA. Please see the Special Instruction below regarding MRC prototypes of interest.

2. Develop medical countermeasures against a broad spectrum of CWA (e.g., nerve and blister agents) by identifying and characterizing compounds or medical strategies

using laboratory and animal models that demonstrate the ability to prevent, interrupt, or terminate the action of CWA.

CATEGORY 2. SPECIAL PROJECTS

The CBMS JPMO is frequently provided funding identified by Congressional committees for special interest developmental efforts relating to medical CBRN countermeasures, enabling technologies, life cycle bioinformatics, health-care delivery; to detection, diagnosis, control or eradication of specified diseases, conditions, or syndromes; or to other initiatives relevant to health needs. Funding of these areas is contemplated to be by grant and is dependent upon Congressional direction and availability of funds.

1. Evaluation of adult-derived stem cells for the repair of tissues following exposure to doses of ionizing radiation sufficient to cause acute radiation syndrome.

2. Evaluation of oral formulations vaccines efficacious against multiple BWA.

3. Comparative performance evaluation of novel, rapid molecular diagnostic assays against unique field isolates of bacterial BW pathogens and food-borne pathogens of military concern.

4. Evaluation of novel pretreatment drugs or compounds which, when taken prior to CWA exposure, increase the efficacy of fielded or developmental medical chemical therapeutic countermeasures.

5. Evaluation of measures to improve the safety or immunogenicity profiles of investigational or licensed vaccines.

CATEGORY 3. DEVELOPMENTAL PROCUREMENT INITIATIVES SUPPORTING MEDICAL CBRN COUNTERMEASURES AND ENABLING TECHNOLOGIES

1. Conduct Good Laboratory Practices (GLP)-compliant *in vivo* studies to demonstrate the safety, efficacy, pharmacokinetics and pharmacodynamics of candidate medical CBRN countermeasures. The study endpoint should be clearly related to the desired benefit in humans in accordance with the FDA "Animal Rule" (21 CFR 314 [I] or 21 CFR 601 [H]).

2. Identifiy and characterize the mechanism of action of candidate medical CBRN countermeasures. Mechanism of action data are required to satisfy the requirements for FDA approval under the "Animal Rule".

3. Conduct of Phase 1 clinical safety studies of potential candidate medical CBRN countermeasures.

4. Evaluate manufacturing processes which may improve the production, shelf life, or stability of candidate or FDA-approved medical CBRN countermeasures.

5. Evaluate novel technologies which a) enable or facilitate efficacious medical logistics cold-chain management and b) eliminate or reduce cold chain requirements for medical CBRN countermeasure storage or shipment.

6. Evaluate emerging life cycle bioinformatics technologies for the ability to improve management processes throughout the discovery, preclinical research, manufacturing, and clinical evaluation phases of pharmaceutical development.

7. Evaluate enabling technologies to enhance/prolong the shelf life of medical CBRN countermeasures currently in the military inventory, including new container-closure systems, wet-dry autoinjectors, or formulations.

8. Evaluate enabling models and simulations, including predictive models and expert systems for population health monitoring.

9. Test and develop products with minimal logistical burden. Activities include development of formulations that require minimal refrigeration, possess long regulatory shelf life, and long operational life once issued. Desired product characteristics would include administration in a single dose, to reduce the need for re-dosing and the ability to use during patient transportation and evacuation as appropriate.

CATEGORY 4. OTHER

Whether under procurement contract, grant or Prototype OT, any other element of developmental effort that would foster or enhance the prospect of potential new products that are consistent with the programmatic mission areas described in The CBMS JPMO Programmatic Mission Area which may be suitable for future competitive advanced development procurements.

CATEGORY 5. DETECTION, DECONTAMINATION AND INFORMATION SOLUTIONS

Identify, mature, and insert science and technology efforts that cut across capabilities, provide substantial improvement to the current state-of-the-art, and add more capability value. The JPEO is specifically interested in research and development of the following capabilities (in order of importance):

- Automated, multi-platform sample preparation
  - Reduce operator error
  - Increase ID confidence
  - Provide independent datapoint
  - Decrease time to obtain results

- Chemical stand-off detection and identification
  - Reduce false positives
  - Enhance performance on low volatility agents
  - Reduce time to detect and ID

- Decontamination solutions:
  - Non-peroxide based
  - For Non-Traditional Agents (NTAs)

- Biological warfare agent stand-off detection and identification
  - Provide 24/7 capability
  - Increase sensitivity
  - Reduce time to warn

- Biological warfare agent point detection
  - Reduced costs
  - Increase sensitivity
  - Increase specificity
  - Layered network capability

- Improved respiratory Toxic Industrial Chemical (TIC) and NTA filtration
  - Increase personnel protection factor
  - NIOSH compliance

- Chemical agent point detection
  - Increase sensitivity
  - Increase specificity
  - Layered network capability

- Fabric technology eliminating the need for chemical and biological protective overgarments and improved collective protection

- Integrated early warning

- Improved radiological detection and identification

- Medical therapeutics and/or prophylaxis for NTAs

- Test and evaluate chemical warfare vapor detectors (CWVD) to validated test methods that are aligned with requirements. Develop and validate additional CWVD test methods and requirements. Assist with CWVD certification and accreditation program by supplying technical recommendations for completing the strategies going forward.

- Open community-of-interest medical and Chemical, Biological, Radiological, and Nuclear (CBRN) data sharing between medical and CBRN information systems

APPENDIX A: TECHNOLOGY READINESS LEVELS FOR MEDICAL PRODUCT DEVELOPMENT

Technology Readiness Level	DoD Description (Acquisition Guidebook 30 Oct 02)	Medical Description[1] (Oct 2004)
1. Basic principles observed and reported.	Lowest level of technology readiness. Scientific research begins to be translated into applied research and development. Examples might include paper studies of a technology's basic properties.	Earliest level of technology readiness. Active monitoring of scientific knowledge base. Scientific findings are reviewed and assessed as a foundation for characterizing new technologies
2. Technology concept and/or application formulated.	Invention begins. Once basic principles are observed, practical applications can be invented. Applications are speculative and there may be no proof or detailed analysis to support the assumptions. Examples are limited to analytic studies.	Focus efforts on practical applications based on basic principles observed. Generation of scientific "paper studies" that review and generate research ideas, hypothesis, and experimental designs for addressing the related scientific issues.
3. Analytical and experimental critical function and/or characteristic proof of concept.	Active research and development is initiated. This includes analytical studies and laboratory studies to physically validate analytical predictions of separate elements of the technology. Examples include components that are not yet integrated or representative.	Research, data collection, and analysis begin in order to: test hypothesis; explore alternative concepts; identify and evaluate critical technologies and components; and research and eventual development of candidate countermeasure(s). Conduct non-clinical studies to support models based on presumed battlefield conditions.
4. Component and/or breadboard validation[2] in laboratory environment.	Basic technological components are integrated to establish that they will work together. This is relatively "low fidelity" compared to the eventual system. Examples include integration of "ad hoc" hardware in the laboratory.	Laboratory research to refine hypothesis and identify relevant parametric data required for technological assessment in a rigorous experimental design. Exploratory study of critical technologies for effective integration into candidate(s). Assess safety and efficacy utilizing animal model(s).

[1] TRL Medical descriptions are generally accepted across the medical acquisition community.
[2] Not "validation" as defined by FDA. FDA-type validations will be done at TRL 6-8 and are needed for licensure.

Technology Readiness Level	DoD Description (Acquisition Guidebook 30 Oct 02)	Medical Description[1] (Oct 2004)
		Propose assays, surrogate markers, and endpoints to be used during non-clinical and clinical studies to evaluate and characterize candidate(s).
5. Component and/or breadboard validation[3] in relevant environment.	Fidelity of breadboard technology increases significantly. The basic technological components are integrated with reasonably realistic supporting elements so it can be tested in a simulated environment. Examples include "high fidelity" laboratory integration of components.	Conduct non-clinical research studies involving data collection and analysis in well-defined systems with highly characterized lots of candidate(s) produced and further development of selected candidates. Develop a robust and reproducible manufacturing process amenable to cGMP. Qualify assays for potency, purity, identity and quality. Qualify surrogate markers for efficacy in animal models.
6. System/sub system model or prototype demonstration in a relevant environment.	Representative model or prototype system, which is well beyond that of TRL 5, is tested in a relevant environment. Represents a major step up in a technology's demonstrated readiness. Examples include testing a prototype in a high-fidelity laboratory environment or in simulated operational environment.	Manufacture, release and stability test GMP pilot lots. Conduct GLP safety studies. Prepare and Submit IND. Conduct Phase 1 clinical trial.
7. System prototype demonstration in an operational environment.	Prototype near or at planned operational system. Represents a major step up from TRL 6, requiring demonstration of an actual prototype in an operational environment such as an aircraft, vehicle, or space. Examples include testing the prototype in a test bed aircraft.	Conduct Phase 2 clinical trial. Establish final dose, dose range, schedule, and route of administration. Data collected, presented, and discussed with FDA at meeting (Type B). Clinical endpoints and supporting animal test plans agreed to by FDA. Complete process validation and initiate consistency lot production.
8. Actual system completed and qualified through	Technology was proven to work in its final form and under expected conditions. In almost all cases, this	Complete production & testing of consistency lots. Conduct Phase 3 clinical trials, if

[3] Not "validation" as defined by FDA. FDA-type validations will be done at TRL 6-8 and are needed for licensure.

Technology Readiness Level	DoD Description (Acquisition Guidebook 30 Oct 02)	Medical Description[1] (Oct 2004)
test and demonstration.	TRL represents the end of true system development. Examples include developmental test and evaluation of the system in its intended weapon system to determine if it meets design specifications.	applicable. Submit BLA/NDA to FDA Obtain FDA approval.
9. Actual system proven through successful mission operations.	Actual application of the technology in its final form and under mission conditions, such as those encountered in operational test and evaluation. Examples include using the system under operational mission conditions.	Post licensure/approval use of product. Fulfill post-licensure commitments, if required.